

WHAT IS CLAIMED IS:

1. A purified complex of p27(Kip1) and FKBP-12.
2. The purified complex of claim 1 in which the proteins are human proteins.
3. A purified complex selected from the group consisting of a complex of a derivative of p27(Kip1) and FKBP-12, a complex of p27(Kip1) and a derivative of FKBP-12, and a complex of a derivative of p27(Kip1) and a derivative of FKBP-12; in which the derivative of p27(Kip1) is able to form a complex with a wild-type FKBP-12 and the derivative of FKBP-12 is able to form a complex with wild-type p27(Kip1).
4. The purified complex of claim 3 in which the derivative of p27(Kip1) or FKBP-12 is fluorescently labeled.
5. A chimeric protein comprising a fragment of p27(Kip1) consisting of at least 6 amino acids fused via a covalent bond to a fragment of FKBP-12 consisting of at least 6 amino acids.
6. The chimeric protein of claim 5 in which the fragment of p27(Kip1) is a fragment capable of binding FKBP-12 and in which the fragment of FKBP-12 is a fragment capable of binding p27(Kip1).
7. The chimeric protein of claim 6 in which the fragment of p27(Kip1) and the fragment of FKBP-12 form a p27(Kip1)•FKBP-12 complex.
8. An antibody which immunospecifically binds the complex of claim 1 or a fragment or derivative of said antibody containing the binding domain thereof.
9. The antibody of claim 8 which does not immunospecifically bind p27(Kip1) or FKBP-12 that is not part of a p27(Kip1)•FKBP-12 complex.
10. An isolated nucleic acid or an isolated combination of nucleic acids comprising a nucleotide sequence encoding p27(Kip1) and a nucleotide sequence encoding FKBP-12.
11. The isolated nucleic acid or isolated combination of nucleic acids of claim 10 which are nucleic acid vectors.
12. The isolated nucleic acid or isolated combination of nucleic acids of claim 11 in which the p27(Kip1) coding sequence and the FKBP-12 coding sequence are operably linked to a promoter.

13. An isolated nucleic acid that comprises a nucleotide sequence encoding the chimeric protein of claim 7.
14. A cell containing a nucleic acid of claim 10, which nucleic acid is recombinant.
15. A cell containing a nucleic acid of claim 12, which nucleic acid is recombinant.
16. A recombinant cell containing a nucleic acid of claim 15, which nucleic acid is recombinant.
17. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the complex of claim 1; and a pharmaceutically acceptable carrier.
18. The pharmaceutical composition of claim 17 in which the proteins are human proteins.
19. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the complex of claim 3; and a pharmaceutically acceptable carrier.
20. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the chimeric protein of claim 5; and a pharmaceutically acceptable carrier.
21. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the chimeric protein of claim 6; and a pharmaceutically acceptable carrier.
22. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the antibody of claim 8 or a fragment or derivative of said antibody containing the binding domain thereof; and a pharmaceutically acceptable carrier.
23. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the antibody of claim 9 or a fragment or derivative of said antibody containing the binding domain thereof; and a pharmaceutically acceptable carrier.
24. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the nucleic acid or combination of nucleic acids of claim 10; and a pharmaceutically acceptable carrier.
25. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the isolated nucleic acid of claim 13; and a pharmaceutically acceptable carrier.

26. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the recombinant cell of claim 14; and a pharmaceutically acceptable carrier.

27. A pharmaceutical composition comprising a therapeutically or prophylactically effective amount of the protein of claim 15; and a pharmaceutically acceptable carrier.

28. A method of producing a complex of p27(Kip1) and FKBP-12 comprising growing a recombinant cell containing the nucleic acid of claim 10 such that the encoded p27(Kip1) and FKBP-12 proteins are expressed and bind to each other, and recovering the expressed complex of p27(Kip1) and FKBP-12.

29. A method of diagnosing or screening for the presence of or a predisposition for developing a disease or disorder characterized by an aberrant level of a complex of p27(Kip1) and FKBP-12, in a subject comprising measuring the level of said complex, RNA encoding p27(Kip1) and FKBP-12, or functional activity of said complex in a sample derived from the subject, in which an increase or decrease in the level of said complex, said RNA encoding p27(Kip1) and FKBP-12, or functional activity of said complex in the sample, relative to the level of said complex, said RNA encoding p27(Kip1) and FKBP-12 or functional activity of said complex found in an analogous sample not having the disease or disorder or a predisposition for developing the disease or disorder, indicates the presence of the disease or disorder or a predisposition for developing the disease or disorder.

30. A kit comprising in one or more containers a substance selected from the group consisting of a complex of p27(Kip1) and FKBP-12, an antibody against said complex, nucleic acid probes capable of hybridizing to RNA of p27(Kip1) and RNA of FKBP-12, or pairs of nucleic acid primers capable of priming amplification of at least a portion of the p27(Kip1) gene and the FKBP-12 gene.

31. A method of treating or preventing a disease or disorder involving aberrant levels of a complex of p27(Kip1) and FKBP-12, in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule or molecules that modulate the function of said complex.

32. The method of claim 31 in which said disease or disorder involves decreased levels of said complex and said molecule or molecules promote the function of the complex of p27(Kip1) and FKBP-12 and are selected from the group consisting of a complex of p27(Kip1) and FKBP-12; a derivative or analog of a complex of p27(Kip1) and FKBP-12, which complex is more stable or more active than the wild type complex; nucleic acids encoding p27(Kip1) and FKBP-12 proteins; and nucleic

acids encoding a derivative or analog of p27(Kip1) and FKBP-12 that form a complex that is more stable or more active than the wild type complex.

33. The method of claim 31 in which said disease or disorder involves increased levels of said complex and said molecule or molecules inhibit the function of said complex and are selected from the group consisting of an antibody against said complex or a fragment or derivative thereof containing the binding region thereof; p27(Kip1) and FKBP-12 antisense nucleic acids; and nucleic acids comprising at least a portion of the *p27(Kip1)* and the *FKBP-12* gene into which a heterologous nucleotide sequence has been inserted such that said heterologous sequence inactivates the biological activity of the at least a portion of the *p27(Kip1)* and *FKBP-12* genes, in which the *p27(Kip1)* and the *FKBP-12* gene portions flank the heterologous sequences so as to promote homologous recombination with genomic *p27(Kip1)* and *FKBP-12* genes.

34. A method of treating or preventing a disease or disorder involving an aberrant level of FKBP-12 in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of FKBP-12.

35. The method of claim 34 in which said disease or disorder involves a decreased level of FKBP-12 and said molecule promotes the function of FKBP-12 and is selected from the group consisting of the FKBP-12 protein, derivative or analog of FKBP-12 that is active in binding p27(Kip1), a nucleic acid encoding FKBP-12, and a nucleic acid encoding a derivative or analog of FKBP-12 that is active in binding p27(Kip1).

36. The method of claim 34 in which said disease or disorder involves an increased level of FKBP-12 and said molecule inhibits FKBP-12 function and is selected from the group consisting of an anti-FKBP-12 antibody or a fragment or derivative thereof containing the binding region thereof, a *FKBP-12* antisense nucleic acid, and a nucleic acid comprising at least a portion of the *FKBP-12* gene into which a heterologous nucleotide sequence has been inserted such that said heterologous sequence inactivates the biological activity of the at least a portion of the *FKBP-12* gene, in which the *FKBP-12* gene portion flanks the heterologous sequence so as to promote homologous recombination with the genomic *FKBP-12* gene.

37. A method of treating or preventing a disease or disorder involving an aberrant level of p27(Kip1) in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of p27(Kip1).

38. The method of claim 37 in which said disease or disorder involves a decreased level of p27(Kip1) and said molecule promotes the function of p27(Kip1) and is selected from the group

consisting of the p27(Kip1) protein, derivative or analog of p27(Kip1) that is active in binding FKBP-12, a nucleic acid encoding p27(Kip1), and a nucleic acid encoding a derivative or analog of p27(Kip1) that is active in binding FKBP-12.

39. The method of claim 37 in which said disease or disorder involves an increased level of p27(Kip1) and said molecule inhibits p27(Kip1) function and is selected from the group consisting of an anti-p27(Kip1) antibody or a fragment or derivative thereof containing the binding region thereof, a p27(Kip1) antisense nucleic acid, and a nucleic acid comprising at least a portion of the *p27(Kip1)* gene into which a heterologous nucleotide sequence has been inserted such that said heterologous sequence inactivates the biological activity of the at least a portion of the *p27(Kip1)* gene, in which the *p27(Kip1)* gene portion flanks the heterologous sequence so as to promote homologous recombination with the genomic *p27(Kip1)* gene.

40. A method for screening a purified complex of p27(Kip1) and FKBP-12, or a derivative of said complex, or a modulator of the activity of said complex for activity in treating or preventing atherosclerosis comprising contacting cultured cells that exhibit an indicator of atherosclerosis *in vitro* with said complex, derivative or modulator; and comparing the level of said indicator in the cells contacted with the complex, derivative, or modulator with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the complex, derivative or modulator has activity in treating or preventing atherosclerosis.

41. A method for screening a purified complex of p27(Kip1) and FKBP-12, or a derivative of said complex, or a modulator of the activity of said complex for activity in treating or preventing an autoimmune disorder comprising contacting cultured cells that exhibit an indicator of a autoimmune disorder *in vitro* with said complex, derivative or modulator; and comparing the level of said indicator in the cells contacted with the complex, derivative, or modulator with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the complex, derivative or modulator has activity in treating or preventing autoimmune disorder.

42. A method for screening a purified complex of p27(Kip1) and FKBP-12, or a derivative of said complex, or a modulator of the activity of said complex for activity in treating or preventing a neurodegenerative disease comprising contacting cultured cells that exhibit an indicator of a neurodegenerative disease *in vitro* with said complex, derivative or modulator; and comparing the level of said indicator in the cells contacted with the complex, derivative, or modulator with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the complex, derivative or modulator has activity in treating or preventing neurodegenerative disease.

43. A method of screening a purified complex of p27(Kip1) and FKBP-12, or a derivative of said complex, or a modulator of the activity of said complex for anti-cancer activity comprising measuring the survival or proliferation of cells from a cell line which is derived from or displays characteristics associated with malignant disorder, which cells have been contacted with the complex, derivative, or modulator; and comparing the survival or proliferation in the cells contacted with the complex, derivative or modulator with said survival or proliferation in cells not so contacted, wherein a lower level in said contacted cells indicates that the complex, derivative or modulator has anti-tumor activity.

44. A method of screening a purified complex of p27(Kip1) and FKBP-12, or a derivative of said complex, or a modulator of the activity of said complex for anti-cancer activity by a method comprising administering the complex, derivative or modulator to a test animal, which test animal has a tumor, or which test animal does not have a tumor and is subsequently challenged with tumor cells or tumorigenic agents; and measuring tumor growth or regression in said test animal, wherein decreased tumor growth or increased tumor regression or prevention of tumor growth in test animals administered said complex, derivative or modulator compared to test animals not so administered indicates that the complex, derivative or modulator has anti-cancer activity.

45. A method for screening a purified complex of p27(Kip1) and FKBP-12, or a derivative of said complex, or a modulator of the activity of said complex for activity in treating or preventing membranous nephropathy disorders comprising contacting cultured cells that exhibit an indicator of a membranous nephropathy disorder *in vitro* with said complex, derivative or modulator; and comparing the level of said indicator in the cells contacted with the complex, derivative, or modulator with said level of said indicator in cells not so contacted, wherein a lower level in said contacted cells indicates that the complex, derivative or modulator has activity in treating or preventing membranous nephropathy disorders.

46. A method for screening a purified complex of p27(Kip1) and FKBP-12, or a derivative of said complex, or a modulator of the activity of said complex for activity in treating or preventing viral infection and associated diseases comprising administering said complex, derivative or modulator to a test animal, which test animal exhibits symptoms of a viral infection or which test animal is predisposed to develop symptoms of a viral infection; and measuring the change in said symptoms of the viral infection after administration of said complex, derivative, or modulator, wherein a reduction in the severity of the symptoms of the viral infection or prevention of the symptoms of the viral infection indicates that the complex, derivative or modulator has activity in treating or preventing viral infection.

47. A method of screening for a molecule that modulates directly or indirectly the formation of a complex of p27(Kip1) and FKBP-12 comprising measuring the levels of said complex formed from p27(Kip1) and FKBP-12 proteins in the presence of said molecule under conditions conducive to formation of the complex; and comparing the levels of said complex with the levels of said complex that are formed in the absence of said molecule, wherein a lower or higher level of said complex in the presence of said molecule indicates that the molecule modulates formation of said complex.

48. A recombinant non-human animal in which both an endogenous *p27(Kip1)* gene and an endogenous *FKBP-12* have been deleted or inactivated by homologous recombination or insertional mutagenesis of said animal or an ancestor thereof.

49. A recombinant non-human animal containing both a *p27(Kip1)* gene and a *FKBP-12* gene, in which the *p27(Kip1)* gene is under the control of a promoter that is not the native *p27(Kip1)* gene promoter and the *FKBP-12* gene is under the control of a promoter that is not the native *FKBP-12* gene promoter.

50. A recombinant non-human animal containing a transgene comprising a nucleic acid sequence encoding the chimeric protein of claim 7.

51. A method of modulating the activity or levels of p27(Kip1) by contacting a cell with, or administering an animal expressing a *p27(Kip1)* gene, a FKBP-12 protein, or a nucleic acid encoding said protein or an antibody that immunospecifically binds said protein or a fragment or derivative of said antibody containing the binding domain thereof.

52. A method of modulating the activity or levels of FKBP-12 by contacting a cell with, or administering an animal expressing a gene encoding said protein, p27(Kip1), or a nucleic acid encoding p27(Kip1), or an antibody that immunospecifically binds p27(Kip1) or a fragment or derivative of said antibody containing the binding domain thereof.

53. A method of modulating the activity or levels of a complex of p27(Kip1) and FKBP-12 by contacting a cell with, or administering an animal expressing and forming said complex, a molecule that modulates the formation of said complex.

54. A method for identifying a molecule that modulates activity of p27(Kip1) or FKBP-12 or a complex of p27(Kip1) and FKBP-12 comprising contacting one or more candidate molecules with p27(Kip1) in the presence of FKBP-12; and measuring the amount of complex that forms between p27(Kip1) and FKBP-12; wherein an increase or decrease in the amount of complex that forms relative

to the amount that forms in the absence of the candidate molecules indicates that the molecules modulate the activity of p27(Kip1) or FKBP-12 or said complex of p27(Kip1) and FKBP-12.

55. The method of claim 54 wherein said contacting is carried out by administering the candidate molecules to the recombinant non-human animal of claim 49.

56. The method of claim 55 wherein said contacting is carried out *in vitro*; and p27(Kip1), FKBP-12, and said candidate molecules are purified.

57. A method for screening a derivative or analog of p27(Kip1) for biological activity comprising contacting said derivative or analog of p27(Kip1) with FKBP-12; and detecting the formation of a complex between said derivative or analog of p27(Kip1) and FKBP-12; wherein detecting formation of said complex indicates that said derivative or analog of p27(Kip1) has biological activity.

58. A method for screening a derivative or analog of FKBP-12 for biological activity comprising contacting said derivative or analog of FKBP-12 with p27(Kip1); and detecting the formation of a complex between said derivative or analog of FKBP-12 and p27(Kip1); wherein detecting the formation of said complex indicates that said derivative or analog of FKBP-12 has biological activity.

59. A method of monitoring the efficacy of a treatment of a disease or disorder characterized by an aberrant level of a complex of p27(Kip1) and FKBP-12 in a subject administered said treatment for said disease or disorder comprising measuring the level of said complex, RNA encoding p27(Kip1) and FKBP-12, or functional activity of said complex in a sample derived from said subject wherein said sample is taken from said subject after the administration of said treatment and compared to (a) said level in a sample taken from said subject prior to the administration of the treatment or (b) a standard level associated with the pretreatment stage of the disease or disorder, in which the change, or lack of change in the level of said complex, said RNA encoding p27(Kip1) and FKBP-12, or functional activity of said complex in said sample taken after the administration of said treatment relative to the level of said complex, said RNA encoding p27(Kip1) and FKBP-12 or functional activity of said complex in said sample taken before the administration of said treatment or to said standard level indicates whether said administration is effective for treating said disease or disorder.

60. A method of treating or preventing atherosclerosis in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of a complex of p27(Kip1) and FKBP-12.

61. A method of treating or preventing autoimmune disease in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of a complex of p27(Kip1) and FKBP-12.

62. A method of treating or preventing neurodegenerative disease in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of a complex of p27(Kip1) and FKBP-12.

63. A method of treating or preventing cancer or a hyperproliferative disorder in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of a complex of p27(Kip1) and FKBP-12.

64. A method of treating or preventing membranous nephropathy or an associated disease in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of a complex of p27(Kip1) and FKBP-12.

65. A method of treating or preventing viral infection or an associated disease in a subject comprising administering to a subject in which such treatment or prevention is desired a therapeutically effective amount of a molecule that modulates the function of a complex of p27(Kip1) and FKBP-12.

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